<PARTICULARS TO APPEAR ON THE OUTER PACKAGE>

{Carton} Blister and DUMA

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Epityl 60mg Flavoured Tablets

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

Each tablet contains:
Phenobarbital 60 mg

3. PACKAGE SIZE

For Blister:
10 tablets
20 tablets
30 tablets
40 tablets
50 tablets
60 tablets
70 tablets
80 tablets
90 tablets
100 tablets
500 tablets
1000 tablets

For DUMA:
100 tablets
500 tablets

4. TARGET SPECIES

Dogs

5. INDICATION(S)

Read the package leaflet before use.

6. ROUTES OF ADMINISTRATION

Oral use.
.

7. WITHDRAWAL PERIODS

Not applicable.

8. EXPIRY DATE

Shelf life of divided tablets: 2 days
EXP {month/year}

9. SPECIAL STORAGE PRECAUTIONS

For blister: Divided tablets should be stored in the original pack. Keep the blister in the outer carton.

For DUMA: Divided tablets should be stored in the original pack. Keep the container in the outer carton.

10. THE WORDS "READ THE PACKAGE LEAFLET BEFORE USE"

Read the package leaflet before use

11. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

12. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

13. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Chanelle Pharmaceuticals Manufacturing Ltd
Loughrea
Co. Galway
Ireland

14. MARKETING AUTHORISATION NUMBER(S)

Vm 08749/5045

15. BATCH NUMBER

BN

16. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.
People with known hypersensitivity to barbiturates should avoid contact with the veterinary medicinal product. Accidental ingestion may cause intoxication and could be fatal, particularly for children. Take utmost care that children do not come in contact with the product.

17. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements.

18. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, IF APPLICABLE

To be supplied only on veterinary prescription.

POM-V

Prescription Only Medicine – Veterinarians

<PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE>

{Label} DUMA

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Epityl 60mg Flavoured Tablets

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

Each tablet contains:
Phenobarbital 60mg

3. TARGET SPECIES

Dogs

4. ROUTES OF ADMINISTRATION

Oral use

5. WITHDRAWAL PERIODS

Not applicable.

6. EXPIRY DATE

Shelf life of divided tablets: 2 days

EXP {month/year}

7. SPECIAL STORAGE PRECAUTIONS

Divided tablets should be stored in the original pack. Keep the container in the outer carton

8. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Chanelle Pharmaceuticals Manufacturing Ltd
Loughrea,
Co. Galway
Ireland

9. BATCH NUMBER

BN

10. PACKAGE SIZE

100 tablets
500 tablets

11. INDICATION(S)

Read the package leaflet before use.

12. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.
Smaller quantities dispensed from a bulk pack should be supplied in a container with a child resistant closure.

13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements.

14. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, if applicable

For animal treatment only. To be supplied only on veterinary prescription.

POM-V

Prescription Only Medicine – Veterinarians

15. MARKETING AUTHORISATION NUMBER(S)

Vm 08749/5045

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

{NATURE/TYPE}

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Epityl

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCE(S)

Phenobarbital 60mg/tablet

3. BATCH NUMBER

BN {number}

4. EXPIRY DATE

EXP {month/year}

5. NAME OF THE MARKETING AUTHORISATION HOLDER

Chanelle Pharmaceuticals Manufacturing Ltd

6. THE WORDS “FOR ANIMAL TREATMENT ONLY”

For animal treatment only.

B. PACKAGE LEAFLET

PACKAGE LEAFLET
Epityl 60mg Tablets for Dogs

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Epityl 60mg Flavoured Tablets for Dogs

2. COMPOSITION

Each tablet contains:
Active substance:
Phenobarbital 60 mg

White, circular tablet with cross breakline on one side
The tablets can be divided into two or four equal parts.

3. TARGET SPECIES

Dogs

4. INDICATIONS FOR USE

Prevention of seizures due to generalized epilepsy in dogs.

5. CONTRAINDICATIONS

Do not use in animals with serious impaired hepatic function.
Do not use in animals with serious renal or cardiovascular disorders.
Do not use in dogs weighing less than 6 kg body weight.
Do not use in case of hypersensitivity to the active substance or to any other barbiturates or to any of the excipients.

6. SPECIAL WARNING(S)

Special warnings:
The decision to start antiepileptic drug therapy with phenobarbital should be evaluated for each individual case and depends on number, frequency, duration and severity of seizures in dogs. Some of the dogs are free of epileptic seizures during the treatment, but some of the dogs show only a seizure reduction, and some of the dogs are considered to be non-responders.

Special precautions for use in animals
Caution is recommended in animals with impaired hepatic and renal function, hypovolemia, anaemia and cardiac or respiratory dysfunction. The chance of hepatotoxic side effects can be diminished or delayed using an effective dose that is as low as possible. Monitoring of hepatic parameters is recommended in case of a prolonged therapy.

It is recommended to assess the clinical pathology of the patient 2-3 weeks after start of treatment and afterwards every 4-6 months, e.g. measurement of hepatic enzymes and serum bile acids. It is important to know that the effects of hypoxia etc. do cause increased levels of hepatic enzymes after a seizure. Phenobarbital may increase the activity of serum alkaline phosphatase and transaminases. These may demonstrate

non-pathological changes, but could also represent hepatotoxicity, liver function tests are recommended. Increased liver enzyme values do not require a dose reduction of phenobarbital if the serum bile acids are in the normal range.

In stabilised epileptic patients, it is not recommended to switch from other phenobarbital formulators to Epityl 60 mg tablets. However, if this cannot be avoided then additional caution should be taken. This includes more frequent plasma concentration sampling to ensure that therapeutic levels are maintained. Monitoring for increased side effects and for hepatic dysfunction should be conducted more regularly until stabilisation is confirmed.
Withdrawal or transition from other types of anti-epileptic therapy should be made gradually to avoid precipitating an increase in the frequency of seizures.

The tablets are flavoured. In order to avoid any accidental ingestion, store tablets out of reach of the animals

Special precautions to be taken by the person administering the veterinary medicinal product to animals

- Barbiturates can cause hypersensitivity. People with known hypersensitivity to barbiturates should avoid contact with the product.
- Accidental ingestion may cause intoxication and could be fatal, particularly for children. Take utmost care that children do not come in contact with the product.
- Phenobarbital is teratogenic and may be toxic to unborn and breastfeeding children; it may affect the developing brain and lead to cognitive disorders. Phenobarbital is excreted in breast milk. Pregnant women, women of childbearing age and women who are breastfeeding should avoid accidental ingestion and prolonged skin contact with the product.
- Keep this product in its original packaging to avoid accidental ingestion.
- It is advisable to wear disposable gloves during administration of the product to reduce skin contact.
- In case of accidental ingestion, seek medical attention immediately, advising medical services of barbiturate poisoning; show the package leaflet or the label to the physician. If possible, the physician should be informed about the time and amount of ingestion, as this information may help to ensure that appropriate treatment is given.
- Each time an unused part-tablet is stored until next use, it should be returned to the open blister space and inserted back into the cardboard box.
- Wash hands thoroughly after use.

Pregnancy and lactation:
Phenobarbital crosses the placental barrier and at higher doses (reversible) withdrawal symptoms in newborns cannot be excluded. Studies in laboratory animals have shown evidence of action of phenobarbital on prenatal growth, especially concerning sexual development. Neonatal bleeding tendencies have been associated with phenobarbital treatment during pregnancy. Administration of Vitamin K to the dam for 10 days before parturition may help to minimise these effects on the foetus. The safety of the product has not been established during pregnancy of dogs. The benefits of treatment may be greater than the potential risks associated with epileptic seizures on the foetus (hypoxia and acidosis). Therefore, in case of pregnancy, termination of antiepileptic treatment is not recommended; however, the dose should be as low as possible.

Phenobarbital is excreted in small amounts in breast milk and during nursing, pups should be monitored carefully for undesired sedative effects. Weaning early may be an option. If somnolence/sedative effects (that could interfere with suckling) appear in nursing newborns, an artificial suckling method should be chosen.
Use during pregnancy and lactation only according to the benefit/risk assessment by the responsible veterinarian.

Interaction with other medicinal products and other forms of interaction:
Phenobarbital will potentially reduce therapeutic levels of a wide range of drugs due to its inducing effect on hepatic enzymes.

A therapeutic dose of phenobarbital for antiepileptic therapy can significantly induce plasma proteins, (such as α1acid glycoprotein, AGP), which bind drugs.
Phenobarbital may reduce the activity of some drugs by increasing the rate of metabolism through induction of drug-metabolising enzymes in liver microsomes. Therefore special attention must be paid to the pharmacokinetics and doses of drugs simultaneously administered. The plasmatic concentration of a range of drugs is decreased in the case of concurrent administration of phenobarbital.
Cimetidine and ketoconazole are inhibitors of hepatic enzymes: concurrent use with phenobarbital can induce an increase of serum concentration of phenobarbital.
Phenobarbital may decrease the absorption of griseofulvin.
Concurrent use with potassium bromide increases the risk of pancreatitis.
Concurrent use with other drugs having a central depressive action can increase the effect of phenobarbital.
Use of phenobarbital tablets in conjunction with primidone is not recommended as primidone is predominantly metabolised to phenobarbital.

Overdose (symptoms, emergency procedures, antidotes):
Toxicity may develop at doses over 20 mg/kg/day or when serum phenobarbital levels rise above 45 microgram/ml.

Symptoms of overdose are:
- depression of the central nervous system demonstrated by signs ranging from sleep to coma,
- respiratory problems,
- cardiovascular problems, hypotension and shock leading to renal failure and death.

In case of overdose remove ingested product from the stomach, for example by lavage. Activated charcoal may be given. Offer respiratory support.

There is no specific antidote, but CNS stimulants, (like Doxapram) may stimulate the respiratory centre. Give oxygen support.

Major Incompatibilities
Not applicable.

7. ADVERSE EVENTS

Dogs:

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Ataxia (incoordination) and sedation[1] Paradoxical hyperexcitability (unusually excitable)[2] Polyuria (increased urination), polydipsia

	(increased thirst) and polyphagia (increased appetite)[3] Hepatotoxicity[4] Pancytopenia and/or neutropenia[5] Low free thyroxine (FT4) or low thyroxine (T4)[6]

[1]: During start of therapy these effects can occur but are usually transitory and disappear in most, but not all, patients with continued medication. Sedation and ataxia often become significant concerns as serum levels reach the higher ends of the therapeutic range.
[2]: Some animals can demonstrate a paradoxical hyperexcitability, particularly after first starting therapy. As this hyperexcitability is not linked to overdosage, no reduction of dosage is needed.
[3]: These effects can occur at average or higher therapeutic active serum concentrations; these effects can be diminished by limiting intake of food.
[4]: High plasma concentrations may be associated with hepatotoxicity.
[5]: Phenobarbital can have deleterious effects on stem cells from bone marrow. Consequences are immunotoxic pancytopenia and/or neutropenia. These reactions disappear after the treatment's withdrawal.
[6]: Treating dogs with phenobarbital may lower their TT4 or FT4 serum levels, however this may not be an indication of hypothyroidism. Treatment with thyroid hormone replacement should only be started if there are clinical signs of the disease.

Reporting adverse events is important. It allows continuous safety monitoring of a product. If you notice any side effects, even those not already listed in this package leaflet, or you think that the medicine has not worked, please contact, in the first instance, your veterinarian. You can also report any adverse events to the marketing authorisation holder or the local representative of the marketing authorisation holder using the contact details at the end of this leaflet, or via your national reporting system.

8. DOSAGE FOR EACH SPECIES, ROUTE(S) AND METHOD OF ADMINISTRATION

For oral administration.
The required dosage will differ to some extent between individuals and with the nature and severity of the disorder.

Tablets must be given at the same time each day and should be co-ordinated with feeding times in a consistent manner to optimise treatment success.

Dogs should be dosed orally, starting with a dose of 2-5mg per kg bodyweight per day. The dose should be divided and administered twice daily.

Steady state serum concentrations are not reached until 1-2 weeks after treatment is initiated. The full effect of the medication does not appear for two weeks and doses should not be increased during this time.

If seizures are not being controlled, the dosage may be increased by 20% at a time, with associated monitoring of serum phenobarbital levels. The phenobarbital serum concentration may be checked after steady state has been achieved, and if it is less than 15µg/ml the dose may be adjusted accordingly. If seizures recur the dose may be raised up to a maximum serum concentration of 45µg/ml. High plasma

concentrations may be associated with hepatotoxicity. Blood samples could be taken at the same time to allow plasma phenobarbital concentration to be determined preferably during trough levels, shortly before the next dose of phenobarbital is due.

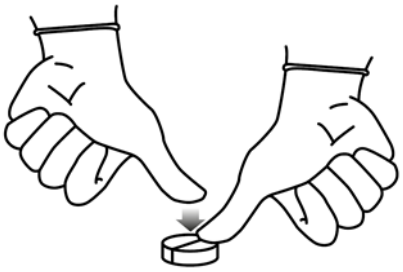
Plasma concentrations should be interpreted in conjunction with the observed response to therapy and a full clinical assessment including monitoring for evidence of toxic effects in each animal.

Clinical data suggests that considerable variation in plasma concentrations of phenobarbital may be observed in some animals. This variation may result in an animal with a trough plasma concentration of phenobarbital below the typical minimum therapeutic level and a peak plasma concentration approaching the maximum level. If the seizure control is inadequate in such animals, care should be taken when increasing the dose as toxic levels may be reached or exceeded. Peak and trough plasma concentrations of phenobarbital may need to be measured in such animals. (Peak plasma concentrations are reached within approximately 3 hours after administration).

If the seizures are not being satisfactorily controlled and if the maximum plasma concentration of phenobarbital is about 40µg/ml, then the diagnosis should be reconsidered and/or a second antiepileptic product (such as bromides) should be added to the treatment protocol.

Tablets can be divided into equal halves or quarters to ensure accurate dosing.
To break a cross scored tablet into quarters, place the tablet on an even surface with the scored side up and apply pressure on the middle with your thumb.

To break a tablet into two halves, place the tablet on an even surface with the scored side up, hold one half of the tablet and press down on the other half.



9. ADVICE ON CORRECT ADMINISTRATION

Steady state serum concentrations are not reached until 1–2 weeks after treatment is initiated. The full effect of the medication does not appear for two weeks and doses should not be increased during this time.
If seizures are not being controlled the dosage may be increased by 20% at a time with associated monitoring of serum phenobarbital levels. The phenobarbital serum concentration may be checked after steady state has been achieved and if it is less than 15 microgram/ml the dose may be adjusted accordingly. If seizures recur the dose may be raised up to a maximum concentration of 45 microgram/ml.
High plasma concentrations may be associated with hepatotoxicity. Blood samples should be taken at the same time to allow plasma phenobarbital concentrations to be determined preferably during trough levels shortly before the next dose of phenobarbital is due.
Withdrawal or transition from other types of anti-epileptic therapy should be made gradually to avoid precipitating an increase in the frequency of seizures.

10. WITHDRAWAL PERIOD

Not applicable.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.
This veterinary medicinal product does not require any special storage conditions.
Shelf-life of divided tablets: 2 days.
Divided tablets should be stored in the original pack. Any divided tablet portions remaining after 2 days should be discarded.
Keep the pack in the outer carton.
Do not use this veterinary medicinal product after the expiry date which is stated on the label and carton after EXP. The expiry date refers to the last day of that month.

12. SPECIAL PRECAUTIONS FOR DISPOSAL

Medicines should not be disposed of via wastewater.
Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements. Ask your veterinary surgeon how to dispose of medicines no longer required. These measures should help to protect the environment.

13. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

POM-V

Prescription Only Medicine – Veterinarians

14. MARKETING AUTHORISATION NUMBERS AND PACK SIZES

Vm 08749/5045

Blister strips (PVC/Aluminium) containing 10 tablets in cartons of 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 500 and 1000 tablets.

White HDPE containers with a polypropylene child resistant cap containing 100 or 500 tablets.

Not all pack sizes and/or types may be marketed.

15. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

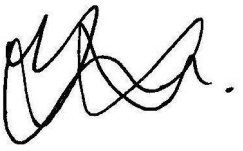
March 2023

16. CONTACT DETAILS

Marketing Authorisation Holder and manufacturer responsible for release and contact details to report suspected adverse reactions:

Chanelle Pharmaceuticals Manufacturing Ltd
Loughrea,
Co. Galway
Ireland.
Telephone: +353 (0)91 841788
vetpharmacoviggroup@chanellegroup.ie

17. OTHER INFORMATION



Approved: 05 June 2023